September 10, 1999

99 SEP 23 A9:37

Dockets Management Branch (HFD-305)
Food and Drug Administration
5630 Fishers Lane., Room 1061
Rockville, MD 20852

Re: Docket No. 98D-0077

Dear Ms. Cook:

We are responding to the request for comments and suggestions regarding the draft document entitled, " Draft Guidance for Industry: *Clinical Development Programs for Drugs, Devices, and Biological Products Intended for the Treatment of Osteoarthritis(OA)*", which was issued on July 15, 1999. We commend the FDA on their continuing effort to provide an OA Guidance document. Attached please find our comments on this version of the draft document. We hope that our recommendations will be taken into consideration in the next draft as they were in the current version.

Please feel free to contact me regarding these comments at (860) 441-8358 if you have any questions.

Sincerely,

R. Wayne Frost, Pharm.D., J.D.
Senior Associate Director
Regulatory Strategy and Registration

98D-0077

C16

Comments on FDA Draft Osteoarthritis Guidance Document

To: FDA Dockets Management Branch (HFD-305)
From: Pfizer Inc.
Re: **Docket #98D-0077** Draft Guidance for Industry: Clinical Development Programs for Drugs, Devices and Biological Products Intended for the Treatment of Osteoarthritis (OA). Federal Register 64:38201; 15 July 1999

Claims for the Treatment of OA

A. Pain and Function:

1. **Pain:** We agree that the claim for pain could stand alone as separate from function. It could be demonstrated by using the Likert or VAS scale. The trial duration should be at least 4 weeks in duration.

2. **Function:** We agree that function could be a separate claim from pain demonstrated by the use of a patient global assessment and a validated measurement of function to include the self-administered questionnaire (WOMAC or Lequesne). We agree that the trial duration should be at least 3 months in order to show that such an effect lasts for a meaningful period of time. We do not believe that x-rays should be required for approval of a symptom claim because they have not been verified to disclose a safety risk. Therefore, the additional x-rays will pose an unnecessary exposure of patients to x-ray radiation in short-term clinical trials. In addition, there should be no requirement for non-signal joint measurement as no methodology exists for assessment. Any significant problem in a non-signal joint would be captured in the Adverse Event reporting.

B. Delay in Structural Progression:

We believe that structural endpoints are sufficient for demonstration of efficacy of a structure modifying drug. There should be no linkage to requirements for demonstration of functional or symptomatic improvement for structure modifying drugs This claim could be demonstrated by improvement in any validated imaging modality to include but not limited to radiographic scores. This would include validated methods to image cartilage integrity, such as arthroscopy or possibly MRI. The duration of the trials should normally be one year to show radiographic changes, but other agents and imaging modalities such as MRI may allow for a shorter trial duration of 6 months. The hierarchical claim structure seems unnecessary and the amount of improvement in the x-ray could be discussed in the Clinical Trials section of the product labeling. With respect to the currently worded claim " *slow JSN by at least a prespecified amount*". We do not believe that a prespecified amount can be determined at this time. We share the view of the Arthritis Advisory Committee that since a clinically relevant minimal difference in JSN has not been determined a

> 50% improvement is unrealistic and too high a hurdle and will inhibit the development of new therapies for patients with OA. The claim should be reworded to, "*delay in deterioration of joint structure*". This claim would be granted if a statistical difference could be demonstrated from the control group, since we cannot determine the "clinically relevant" change at this time. We support the demonstration of this effect in the slowing of the loss of knee or hip JSN and generalizing to the other joints, as recommended in the guidance.

C. <u>Prevention of OA</u>:

There are inherent methodological problems with this claim as discussed by the Arthritis Advisory Committee. These problems center around the definition of "new OA". However, if a sponsor can find a suitable definition for onset of OA and a suitable methodology for showing its delay, such a claim should not be precluded.

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